Immune-Response against Biofilm

A biofilm is an accumulation of microorganisms (bacteria, fungi, and/or protozoa, with associated bacteriophages and other viruses) embedded in a polysaccharide matrix and adherent to solid a biologic or non-biologic surface. Biofilms are clinically important, accounting for over 80 percent of microbial infections in the body. Examples include: infections of the oral soft tissues, teeth and dental implants; middle ear; gastrointestinal tract; urogenital tract; airway/lung tissue; eye; urinary tract prostheses , The biofilm-associated microorganisms tend to be far more resistant to antimicrobial agents and make it particularly difficult for the host immune system to render an appropriate response.

The mechanisms that enable bacteria in biofilms to resist host defenses are less well characterized, but include :

(i) limited penetration of leukocytes and their bactericidal products into the biofilm

(ii) global response regulators and quorum sensing activities that increase resistance to leukocytes (iii) decreased ability of leukocytes to engulf biofilm bacteria

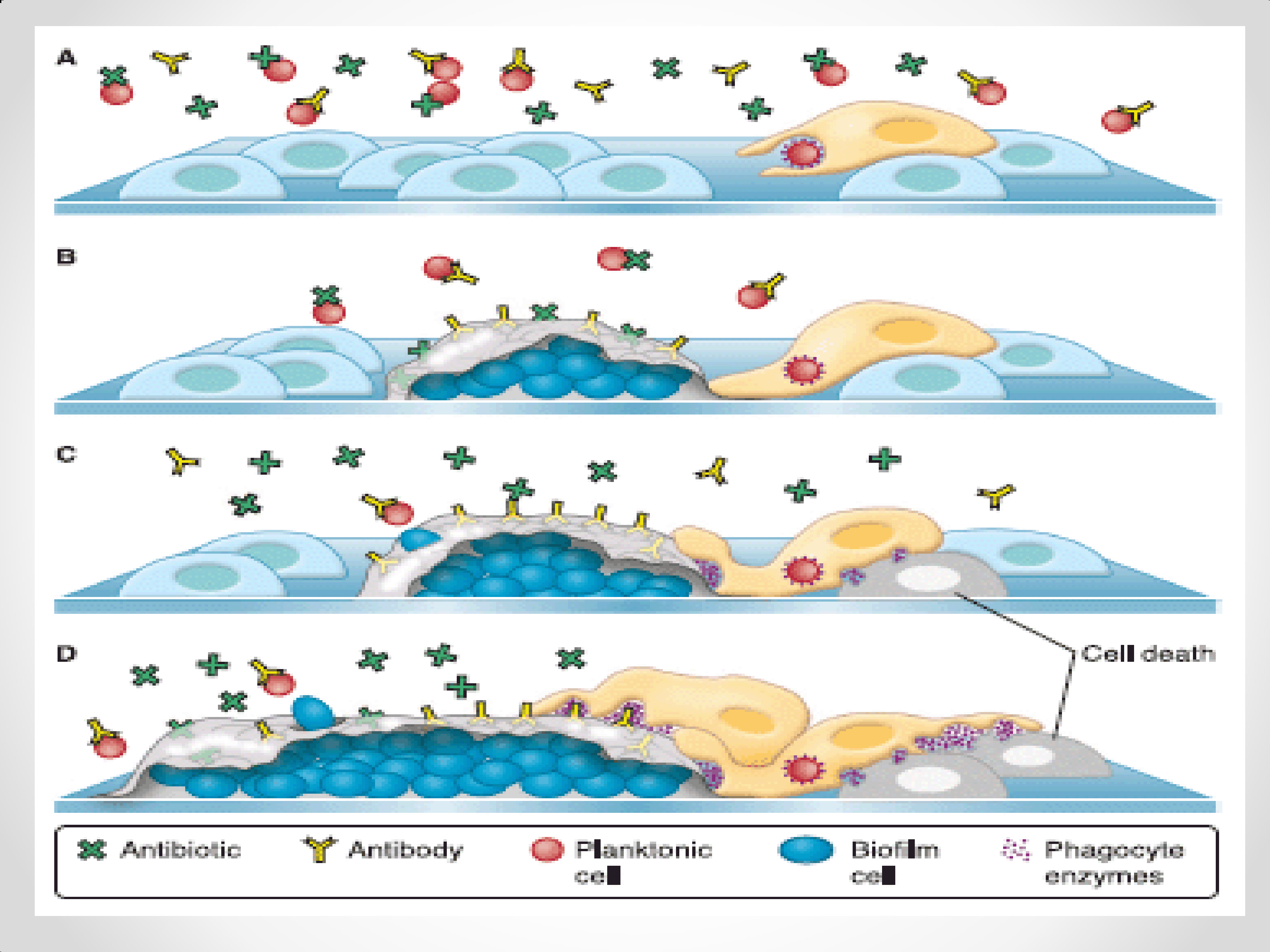
(iv) genetic switches that increase resistance of bacterial cells in biofilms to the immune system

(v) suppression of leukocyte activity through effector regulation

Human leukocyte interactions with medically relevant bacterial biofilms under conditions that mimic physiological shear. Biofilm act as physical barrier around the respective biofilm microcommunities serves as a potential resistance mechanism, but some time human leukocytes do penetrate *S. aureus* biofilms . Therefore, other properties of biofilms provide the basis for the inability of the host immune system to eliminate these infections.

in vivo, human leukocytes are able to more effectively penetrate the biofilm, possibly by using the nutrient/flow channels that exist in a mature biofilm. Additionally, we have previously demonstrated that biofilms are more like an extremely porous hydrogel than a solid, rigid structure. Moreover, the fact that the leukocytes were able to penetrate the biofilm but unable to engulf the bacteria present in the biofilm suggests that other mechanisms that inhibit normal leukocyte function

antibacterial mechanism within the innate immune system depends on phagocytes, including neutrophils and macrophages, engulfing and killing microorganisms. This defensive mechanism is very effective against many types of pathogens when they live as planktonic, individual organisms. Normal mucosal surfaces resist biofilm infections despite continual exposure to commensal and pathogenic bacteria



A
B
C
D
Cell death
Antibiotic
Antibody
Planktonic cell
Biofilm cell
Phagocyte enzymes

Frustrated phagocytosis a phenomenon occur when macrophages and neutrophils encounter but cannot engulf bacteria in biofilms, they are activated and secrete toxic compounds that damage nearby healthy host tissues

biofilms modulate the effectiveness of those effector molecules. When neutrophils encounter P. aeruginosa biofilms, they produce less superoxide compared to when they encounter the planktonic form of this pathogen. Other oxygen- dependent (nitric oxide) and oxygen-independent host-neutrophil responses (lysozyme, lactoferrin) are also reduced in magnitude in response to P. aeruginosa biofilms

In response to incubation with 2-day-old biofilms grown under static conditions, leukocytes produced increased quantities of interleukin-1β (IL-1β), IL-12 and gamma interferon (IFN-γ) that indicate the presence of high Th1 response but this response is less effective against bacteria in biofilm .

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Alginate is an important extracellular component of mucoid strains of P. aeruginosa scavenges hypochlorite, reduces polymorphonuclear chemotaxis, inhibits activation of complement, and decreases phagocytosis by neutrophils and macrophages. But , antibodies that are directed against alginate aid in cell-mediated killing of P. aeruginosa biofilms, comparable antibodies from CF patients fail to do so.

alginate upregulates two Th1-type cytokines, interleukin- 12 (IL-12) and tumor necrosis factor-a (TNF-a). However, even though alginate elicits the host to produce higher levels of these Th1 cytokines, the biofilm bacteria have mechanisms that block or inhibit cell-mediated killing

mononuclear cells (lymphocytes and monocytes) and neutrophils were required for killing of these biofilm bacteria and that cytokines from these cells were important in the production of bactericidal lactoferrin. Although killing of the bacterial biofilms did not involve phagocytosis, appropriate cytokines were vital to generate a killing response. Both interferon-a (IFN-aγ) and TNF-a were required for optimal killing, with the latter cytokine especially important for eliciting neutrophil- mediated killing by inducing release of lactoferrin.